Important information. Please read carefully.

ASLENE™

ORLISTAT 120MG
Capsule

COMPOSITION
Each capsule contains Orlistat 120mg.

PHARMACODYNAMICS
Orlistat is a potent, specific and long-acting inhibitor of gastrointestinal lipases. It exerts its therapeutic activity in the lumen of the stomach and small intestine by forming a covalent bond with the active serine site of the gastric and pancreatic lipases. The inactivated enzyme is thus unavailable to hydrolyse dietary fat, in the form of triglycerides, into absorbable free fatty acids and monoglycerides.

PHARMACOKINETICS
Absorption
The extent of absorption of orlistat was minimal. Plasma concentrations of intact orlistat were non-measurable (< 5 ng/ml) following a single oral administration 360mg of orlistat.
In general, after long term treatment at therapeutic doses, detection of intact orlistat in plasma was sporadic and concentrations were extremely low (< 10 ng/ml or 0.02 µmol), with no evidence of accumulation, which is consistent with minimal absorption.

Distribution
The volume of distribution cannot be determined because the drug is minimally absorbed and has no defined systemic pharmacokinetics. In vitro orlistat is > 99 % bound to plasma proteins (lipoproteins and albumin were the major binding proteins). Orlistat minimally partitions into erythrocytes.

Metabolism
Two major metabolites, M1 (4-member lactone ring hydrolysed) and M3 (M1 with N-formyl leucine moiety cleaved), accounted for approximately 42 % of the total plasma concentration.

M1 and M3 have an open beta-lactone ring and extremely weak lipase inhibitory activity (1000 and 2500 fold less than orlistat respectively). In view of this low inhibitory activity and the low plasma levels at therapeutic doses (average of 26 ng/ml and 108 ng/ml respectively), these metabolites are considered to be pharmacologically inconsequential.

Elimination
Faecal excretion of the unabsorbed drug was the major route of elimination. Approximately 97 % of the administered dose was excreted in faeces and 83 % of that as unchanged orlistat.

The cumulative renal excretion of total orlistat-related materials was < 2 % of the given dose. The time to reach complete excretion (faecal plus urinary) was 3 to 5 days. The disposition of orlistat appeared to be similar between normal weight and obese volunteers. Orlistat, M1 and M3 are all subject to biliary excretion.

Pharmacokinetics in Special Populations
Plasma concentrations of orlistat and its metabolites M1 and M3 were similar in paediatric patients compared to those found in adults at the same dose level. Daily fecal fat excretions were 27% and 7% of dietary intake in orlistat and placebo treatment groups, respectively.

INDICATIONS
Aslene is indicated in conjunction with a mildly hypocaloric diet for the treatment of obese patients with a body mass index (BMI) greater or equal to 30 kg/m^2, or overweight patients (BMI ≥ 28 kg/m^2) with risk factors associated with obesity.

Aslene is effective in weight loss, weight maintenance and prevention of weight regains. Treatment with Aslene results in an improvement of risk factors and comorbidities associated with obesity, including hypercholesterolemia, noninsulin dependent diabetes mellitus (NIDDM), impaired glucose tolerance, hyperinsulinemia, hypertension and in a reduction of visceral fat.

The use of Aslene in type 2 diabetic patients who are overweight (BMI ≥ 28 kg/m^2) or obese (BMI ≥ 30 kg/m^2), in conjunction with a mildly hypocaloric diet, provides additional glycemic control when used in combination with antidiabetic agents such as metformin, sulfonylurea and/or insulin.

Treatment with Aslene should only be started if diet alone has previously produced a weight loss of at least 2.5kg over a period of 4 consecutive weeks. Treatment with Aslene should be discontinued after 12 weeks if patients have been unable to lose at least 5 % of the body weight as measured at the start of therapy.

DOSAGE AND ADMINISTRATION
Adults
The recommended dose of Aslene is one 120mg capsule with each main meal (during or up to one hour after the meal). If a meal is missed or contains no fat, the dose of Aslene may be omitted.

The patient should be on a nutritionally balanced, mildly hypocaloric diet that contains approximately 30% of calories from fat. The daily intake of fat, carbohydrate and protein should be distributed over three main meals.
Doses above 120 mg three times daily have not been shown to provide additional benefit.

Special populations
The effect of orlistat in patients with hepatic and/or renal impairment, children under the age of 12, and elderly patients has not been studied.

CONTRAINDICATIONS
Aslene is contraindicated in patients with chronic malabsorption syndrome, cholestasis and in patients with known hypersensitivity to orlistat or any component of this product.

WARNINGS AND PRECAUTIONS
In order to ensure adequate nutrition, the use of a multivitamin supplement (Vitamin A, D, E and K, and beta-carotene) should be considered.

Patients should be advised to adhere to dietary guidelines (see Dosage and Administration).

A reduction in cyclosporin plasma levels has been observed when orlistat is co-administered. Therefore it is recommended to monitor more frequently than usual the cyclosporin plasma levels when orlistat is co-administered.

A potential reduced therapeutic effect of amiodarone is possible due to the complex pharmacokinetics of amiodarone.

The possibility of experiencing gastrointestinal adverse reactions (see Side Effects) may increase when orlistat is taken with a diet high in fat (e.g. in a 2000 kcal/day diet, >30% of calories from fat equates to >67g of fat). The daily intake of fat should be distributed over three main meals. If orlistat is taken with any one meal very high in fat, the possibility of gastrointestinal effects may increase.

Weight loss induced by orlistat is accompanied by improved metabolic control in type 2 diabetics which might allow or require reduction in the dose of oral hypoglycemic medication (eg. sulfonylureas).

Substantial weight loss may increase the risk of cholelithiasis.

Coagulation parameters should be monitored in patients treated with concomitant oral anticoagulants.

Cases of rectal bleeding have been reported with orlistat. Prescribers should investigate further in case of severe and/or persistent symptoms.

DRUG INTERACTIONS
Cyclosporin
A decrease in cyclosporin plasma levels has been observed when orlistat is co-administered. This can lead to a decrease of immunosuppressive efficacy. Therefore more frequent monitoring of cyclosporin blood levels is recommended when orlistat is co-administered.

Acarbose
In the absence of pharmacokinetic interaction studies, the concomitant administration of orlistat with acarbose should be avoided.

Oral anticoagulants
When warfarin or other anticoagulants are given in combination with orlistat, international normalised ratio (INR) values should be monitored.

Fat soluble vitamins
Treatment with orlistat may potentially impair the absorption of fat-soluble vitamins (A, D, E and K). If a multivitamin supplement is recommended, it should be taken at least two hours after the administration of orlistat or at bedtime.

Amiodarone
Clinical and ECG monitoring are warranted in patients receiving concomitant amiodarone treatment.

Lack of interactions
No interactions with amitriptyline, atorvastatin, biguanides, digoxin, fibrates, fluoxetine, losartan, phenytoin, oral contraceptives, phentermine, pravastatin, warfarin, nifedipine Gastrointestinal Therapeutic System (GITS), nifedipine slow release, sibutramine or alcohol have been observed.

Orlistat may indirectly reduce the availability of oral contraceptives and lead to unexpected pregnancies in some individual cases. An additional contraceptive method is recommended in case of severe diarrhoea.

PREGNANCY AND LACTATION
Use during pregnancy
Orlistat is not recommended for use during pregnancy in the absence of clinical data.

Use during lactation
Orlistat should not be taken during breast-feeding. The secretion of orlistat in human breast milk has not been investigated.

SIDE EFFECTS
Adverse reactions to orlistat are largely gastrointestinal in nature. Consumption of diet low in fat will decrease the likelihood of experiencing adverse gastrointestinal events. These adverse gastrointestinal reactions are generally mild and transient. They occurred early in treatment (within 3 months) and most patients experienced only one episode.

Gastrointestinal reactions
Abdominal pain/discomfort, oily spotting from the rectum, flatus with discharge, faecal urgency, fatty/oily stool, flatulence, liquid stools, oily evacuation, increased defecation, rectal pain/discomfort, soft stools, faecal incontinence, tooth disorder, gingival disorder.

Other adverse reactions
Headache, upper respiratory infection, lower respiratory infection, urinary tract infection, influenza, fatigue, menstrual irregularity and anxiety.
Unique treatment adverse events observed in obese type 2 diabetic patients were hypoglycemia (very common) and abdominal distension (common).

Hypersensitivity (e.g. pruritus, rash, urticaria, angioedema, bronchospasm and anaphylaxis), bullous eruptions, increase in liver transaminases and in alkaline phosphatase and exceptional cases of hepatitis that may be serious. No causal relationship or physiopathological mechanism between hepatitis and orlistat therapy has been established.

Decreased prothrombin, increased INR and unbalanced anticoagulant treatment resulting in change of haemostatic parameters may occur in patients treated concomitantly with anticoagulants.

SYMPTOMS AND TREATMENT FOR OVERDOSAGE
Single doses of 800mg orlistat and multiple doses of up to 400mg tid for 15 days have been studied in normal weight and obese subjects without significant adverse findings. In addition, doses of 240mg tid have been administered to obese patients for 6 months without significant increase of adverse findings.

Orlistat overdose cases are similar to those reported with recommended dose.

Should a significant overdose of orlistat occur, it is recommended that the patient be observed for 24 hours. Any systemic effects attributable to the lipase-inhibiting properties of orlistat should be rapidly reversible.

SHELF-LIFE
The expiry date is indicated on the packaging.

STORAGE CONDITION
Store below 25°C and away from excessive heat, light and moisture. Do not keep in the bathroom.

PRODUCT DESCRIPTION
Blue/Blue hard gelatin capsule printed with "XSP". Available as blister strips of 10's in packing of 30 capsules per box.

KEEP OUT OF REACH OF CHILDREN
JAUHI DARI KANAK-KANAK

For further information, please consult your pharmacist or physician.

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Manufactured and Marketed by:
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